

LANGUAGE: Unavailable

AB Sections of ingots from 4 heats of high-Cr steel, 3 of which contain 0.25-1.97% Ti, were studied macro- and microscopically. Ti causes grain refinement and eliminates ingotism when present in amounts greater than 1.11% Ti. 1.97% Ti, and possibly less, with C (0.20-0.25%), eliminates both air-hardening and hardenability, except that water quenching from 2100°F. may cause slight hardening. The 1.11% Ti alloy may be considered as a C-free, high Cr-Fe alloy with TiC inclusions, since Ti has combined with all C present. TiC is soluble at 2500°F. and therefore subject to rearrangement by heat treatment; the steel is not hardened by their solution. Macro- and microphotographs are included to show typical structures obtained by various heat treatments.

=> d his

(FILE 'HOME' ENTERED AT 14:39:16 ON 14 AUG 2007)

FILE 'CAPLUS' ENTERED AT 14:40:47 ON 14 AUG 2007  
E NANOTUBE

L1 192 S CARBON NANOTUB? (L) THU/RL  
L2 1 S L1 AND PY<=2001  
L3 80 S NANOPART? AND WATER INSOLUBLE AND (THU OR PAC OR DMA OR PKT)/  
L4 24 S L3 AND PY<=2001  
L5 11 S L4 AND PARTICLE SIZE  
L6 5 S 1-11 TI

=> d 15 1-11 ibib abs

L5 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:485154 CAPLUS  
DOCUMENT NUMBER: 141:42911  
TITLE: Protein stabilized pharmacologically active agents, methods for the preparation thereof, and methods for the use thereof  
INVENTOR(S): Desai, Neil P.; Tao, Chunlin; Yang, Andrew; Louie, Leslie; Yao, Zhiwen; Soon-Shiong, Patrick; Magdassi, Shlomo  
PATENT ASSIGNEE(S): American Bioscience, Inc., USA  
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 198,082, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 19  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6749868	B1	20040615	US 1999-316642	19990521
US 5439686	A	19950808	US 1993-23698	19930222 <--
CN 1839806	A	20061004	CN 2006-10001279	19940222
US 5560933	A	19961001	US 1995-412726	19950329 <--
US 5916596	A	19990629	US 1996-720756	19961001 <--
CA 2371912	A1	20001130	CA 2000-2371912	20000519 <--
WO 2000071079	A2	20001130	WO 2000-US13954	20000519 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 200050359	A	20001212	AU 2000-50359	20000519 <--
AU 784416	B2	20060330		
EP 1178786	A1	20020213	EP 2000-932669	20000519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6537579	B1	20030325	US 2000-574763	20000519
AU 2006202836	A1	20060727	AU 2006-202836	20060630
PRIORITY APPLN. INFO.:			US 1993-23698	A2 19930222
			US 1995-412726	A2 19950329
			US 1996-720756	A3 19961001
			US 1998-198082	B2 19981123
			US 1993-35150	A 19930326
			CN 1994-191236	A3 19940222
			US 1994-200235	A2 19940222
			US 1997-51021P	P 19970627
			US 1997-926155	A2 19970909
			WO 1998-US13272	W 19980626
			US 1999-316642	A 19990521
			US 2000-446783	A2 20000516
			AU 2000-50359	A 20000519
			WO 2000-US13954	W 20000519

AB In accordance with the present invention, there are provided compns. and methods useful for the in vivo delivery of substantially water insol. pharmacol. active agents (such as the anticancer drug paclitaxel) in which the pharmacol. active agent is delivered in the form of suspended particles coated with protein (which acts as a stabilizing agent). In particular, protein and pharmacol. active agent in a biocompatible dispersing medium are subjected to high shear, in the absence of any conventional surfactants, and also in the absence of any polymeric core material for the particles. The procedure yields particles with a diameter of less than about 1  $\mu$ . The use of specific composition and preparation conditions (e.g., addition of a polar solvent to the organic phase), and

careful election of the proper organic phase and phase fraction, enables the reproducible production of unusually small nanoparticles of less than 200 nm diameter, which can be sterile-filtered. The particulate system produced according to the invention can be converted into a redispersible dry powder comprising nanoparticles of water-insol. drug coated with a protein, and free protein to which mols. of the pharmacol. agent are bound. This results in a unique delivery system, in which part of the pharmacol. active agent is readily bioavailable (in the form of mols. bound to the protein), and part of the agent is present within particles without any polymeric matrix therein.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:235427 CAPLUS  
 DOCUMENT NUMBER: 138:243333  
 TITLE: Pharmaceutical compositions for anticancer drug delivery  
 INVENTOR(S): Desai, Neil P.; Soon-Shiong, Patrick  
 PATENT ASSIGNEE(S): American Bioscience, Inc., USA  
 SOURCE: U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 446,783.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 19  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 6537579	B1	20030325	US 2000-574763	20000519
US 5439686	A	19950808	US 1993-23698	19930222 <--
US 5498421	A	19960312	US 1994-200235	19940222 <--
CN 1839806	A	20061004	CN 2006-10001279	19940222
US 5560933	A	19961001	US 1995-412726	19950329 <--
US 5916596	A	19990629	US 1996-720756	19961001 <--
US 6096331	A	20000801	US 1997-926155	19970909 <--
WO 9900113	A1	19990107	WO 1998-US13272	19980626 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6749868	B1	20040615	US 1999-316642	19990521
WO 2001089522	A1	20011129	WO 2001-US15993	20010518 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1337249	A1	20030827	EP 2001-937499	20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:				
		US 1993-23698	A2	19930222
		US 1994-200235	A2	19940222
		US 1995-412726	A2	19950329
		US 1996-720756	A3	19961001
		US 1997-51021P	P	19970627
		US 1997-926155	A2	19970909
		WO 1998-US13272	W	19980626
		US 1998-198082	B2	19981123
		US 1999-316642	A2	19990521
		US 2000-446783	A2	20000516
		US 1993-35150	A2	19930326
		CN 1994-191236	A3	19940222
		US 1995-485448	A2	19950607
		US 2000-574763	A1	20000519
		WO 2001-US15993	W	20010518

AB Compns. for the in vivo delivery of substantially water-insol. drugs (e.g., anticancer drug paclitaxel) in which the drug is delivered in the form of suspended particles coated with protein (which acts as a stabilizing agent) are disclosed. In particular, the protein and the drug in a biocompatible dispersing medium are subjected to high shear, in the absence of any conventional surfactants, and also in the absence of any polymeric core material for the particles. The procedure yields particles with a diameter of <1  $\mu$ . The use of specific composition and preparation conditions (e.g., addition of a polar solvent to the organic phase), and careful election of the proper organic phase and phase fraction, enables the reproducible production of unusually small nanoparticles of <200 nm diameter, which can be sterile-filtered. The particulate system produced according to the invention can be converted into a redispersible dry powder comprising nanoparticles of water-insol. drug coated with a protein, and free protein to which mols. of the drug are bound. This results in a unique delivery system, in which part of the drug is readily bioavailable (in the form of mols. bound to the protein),

and part of the agent is present within. When reconstituted with 0.9% NaCl injection, paclitaxel (ABI-007) forms a colloidal suspension of paclitaxel stabilized with human albumin. The formulation contains no other added excipients. The sterility of the product is assured by an aseptic manufacturing process and sterile filtration. Cmpns. in polymeric or glass containers were diluted with sterile normal saline to concns. of 0.5, 1, 5, 10, and 15 mg/mL. and stored at room temperature and under refrigerated conditions. The compns. were homogeneous and stable for at least 24 h-3 days under these conditions. Particle size

measurements performed at several time points indicated no change in size distribution. No precipitation was seen under these conditions. The diluted compns. were stable in the presence of different polymeric materials such as teflon, silastic, polyethylene, Tygon, and other standard infusion tubing materials. ABI-007 exhibited antitumor activity in L1210 murine leukemia cells. The IC<sub>50</sub> for ABI-007 was 0.014 µg/mL.

REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:347081 CAPLUS

DOCUMENT NUMBER: 138:78305

TITLE: Meltrex-formulations containing solid solutions of nearly insoluble drugs: Formation of nanoparticles on dissolution in water

AUTHOR(S): Rosenberg, J.; Berndl, G.; Breitenbach, J.; Liepold, B.; Maegerlein, M.; Reinhold, U.

CORPORATE SOURCE: The Drug Delivery Business Unit of Knoll AG, Knoll Soliqs - The Drug Delivery Business Unit of Knoll AG, Ludwigshafen, D-67061, Germany

SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 1, 738-739. Controlled Release Society: Minneapolis, Minn.

CODEN: 69CNY8

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Water-insol. emulsifiers like Sorbitan fatty acid esters (Span) were formulated together with sparingly water-soluble drug compds. by melt extrusion of a solid water-soluble polymer matrix consisting of PVP/VA-Copolymer (Meltrex tablets). Depending on the Span type used the formulations showed self-emulsifying properties on dissoln. in water, creating emulsions with droplet size in the nano- and micrometer range.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:271054 CAPLUS

DOCUMENT NUMBER: 136:284473

TITLE: Methods and compositions for enhancing the bioadhesive properties of polymers

INVENTOR(S): Jacob, Jules S.; Mathiowitz, Edith

PATENT ASSIGNEE(S): Brown University Research Foundation, USA

SOURCE: U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 135,705.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
----- US 6368586	----- B1	----- 20020409	----- US 2000-535421	----- 20000327

US 5985312	A	19991116	US 1996-592565	19960126 <--
US 6123965	A	20000926	US 1998-135705	19980818 <--
PRIORITY APPLN. INFO.:			US 1996-592565	A3 19960126
			US 1998-135705	A2 19980818

AB Methods and compns. are provided for enhancing the bioadhesive properties of polymers used in drug delivery devices. The bioadhesive properties of a polymer are enhanced by incorporating a water-insol. metal compound, e.g., a metal oxide, in an amount effective to improve, upon exposure of the metal compound at a surface of the polymer, adhesion of the polymer to the mucosal membrane. The metal compds. can be incorporated within a wide range of polymers including proteins, polysaccharides and synthetic biocompatible polymers. In one embodiment, metal oxides can be incorporated within polymers used to form or coat drug delivery devices, such as microspheres, which contain a drug or diagnostic agent. The metal oxides can be provided in the form of a fine dispersion of particles on the surface of a polymer that coats or forms the devices, which enhances the ability of the devices to bind to mucosal membranes. The polymers, for example in the form of microspheres, have improved ability to adhere to mucosal membranes, and thus can be used to deliver a drug or diagnostic agent via any of a range of mucosal membrane surfaces including those of the gastrointestinal, respiratory, excretory and reproductive tracts. For example, polystyrene (2 KDa) microspheres containing 40% ferric oxide (weight/weight) were prepared by solvent evaporation in the size range 10-300  $\mu\text{m}$ . A test using a rat everted intestinal sac bioassay showed that 38% of the initial dose of microspheres was bound to small intestine.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:868221 CAPLUS

DOCUMENT NUMBER: 136:11150

TITLE: Compositions and methods for administration of antitumor agents

INVENTOR(S): Desai, Neil P.; Soon-Shiong, Patrick

PATENT ASSIGNEE(S): American Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089522 A1		20011129WO	2001-US15993	20010518
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR				

PRIORITY APPLN. INFO.: US 2000-574763 20000519

AB In accordance with the present invention, there are provided compns. and methods useful for the in vivo delivery of substantially water insol. drugs (such as the anticancer drug, paclitaxel) in which the drug is delivered in the form of suspended particles coated with protein (which acts as a stabilizing agent). In particular, protein and drug in a biocompatible dispersing medium are subjected to high shear, in the absence of any conventional surfactants, and also in the absence of any polymeric core material for the particles. The procedure yields particles with a diameter of  $< 1 \mu$ . The use of specific composition and preparation

conditions (e.g., addition of a polar solvent to the organic phase), and careful

selection of the proper organic phase and phase fraction, enables the reproducible production of unusually small nanoparticles of less than 200 nm diameter, which can be sterile-filtered. The particulate system produced according to the invention can be converted into a redispersible dry powder comprising nanoparticles of water-insol. drug coated with a protein, and free protein to which mols. of the drug are bound. This results in a unique delivery system, in which part of the pharmacol. active agent is readily bioavailable (in the form of mols. bound to the protein), and part of the agent is present within. Thus, ABI-007 formed a colloidal suspension of paclitaxel stabilized with human albumin. The compound can be administered at 30, 100, or 300 mg.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:472465 CAPLUS

DOCUMENT NUMBER: 135:66243

TITLE: Process for producing nanometer particles by fluidized-bed spray-drying

INVENTOR(S): Kerkhof, Nicholas J.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045677	A1	20010628	WO 2000-US34606	20001219 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395129	A1	20010628	CA 2000-2395129	20001219 <--
EP 1239844	A1	20020918	EP 2000-986607	20001219
EP 1239844	B1	20050608		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518038	T	20030603	JP 2001-546416	20001219
AU 778931	B2	20041223	AU 2001-22814	20001219
AT 297196	T	20050615	AT 2000-986607	20001219
ES 2240222	T3	20051016	ES 2000-986607	20001219
MX 2002PA06079	A	20040823	MX 2002-PA6079	20020619
US 2003211162	A1	20031113	US 2002-168520	20021018
US 7078057	B2	20060718		
US 2006210640	A1	20060921	US 2006-438240	20060521
PRIORITY APPLN. INFO.:			US 1999-172573P	P 19991220
			WO 2000-US34606	W 20001219
			US 2002-168520	A2 20021018

AB Nanometer particles of poorly water-soluble or substantially water-insol. compound are produced by finely-spraying a non-aqueous solution of said compound into a heated and fluidized bed of carrier excipient. The resulting product consists of a free flowing mixture of relatively large particles of carrier excipient and nanometer sized particles (<3 µm) of the compound. Approx. 100 g ganaxolone was dissolved in 5 kg ethanol with

slight warming to 30°. The solution was sprayed into 1 kg of spray-dried lactose NF in a fluidized-bed system equipped with a 6" Wurster column. The spray rate was 34-41 mL/min. The static inlet pressure was 2.5-8 bar. The resulting ganaxolone powder mixture was free-flowing and contained 63 mg ganaxolone/g of powder. The ganaxolone particle size in the mixture was determined by a laser diffraction technique by using photocorrelation spectroscopy. The ganaxolone had a volume-weighted mean diameter of 660 nm.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2001:472463 CAPLUS  
DOCUMENT NUMBER: 135:66241  
TITLE: Process for producing nanometer particles by fluid-bed spray-drying  
INVENTOR(S): Kerkhof, Nicholas J.; Ong, John T. H.  
PATENT ASSIGNEE(S): Cogensys, Inc., USA  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045674	A1	20010628	WO 2000-US34479	20001219 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
ES 2240222	T3	20051016	ES 2000-986607	20001219

PRIORITY APPLN. INFO.: US 1999-172573P P 19991220

AB Nanometer particles of poorly water-soluble or substantially water-insol. compound are produced by finely-spraying a non-aqueous solution of said compound into a heated and fluidized bed of carrier excipient. The resulting product consists of a free flowing mixture of relatively large particles of carrier excipient and nanometer sized particles (<1 µm) of compound. Approx. 100 g ganaxolone was dissolved in 5 kg ethanol with slight warming to 30°. The solution was sprayed into 1 kg of spray-dried lactose NF in a fluidized-bed system equipped with a 6" Wurster column. The spray rate was 34-41 mL/min. The static inlet pressure was 2.5-8 bar. The resulting ganaxolone powder mixture was free-flowing and contained 63 mg ganaxolone/g of powder. The ganaxolone particle size in the mixture was determined by a laser diffraction technique by using photocorrelation spectroscopy. The ganaxolone had a volume-weighted mean diameter of 660 nm.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2000:841943 CAPLUS  
DOCUMENT NUMBER: 134:21448  
TITLE: Preparation of protein-stabilized pharmaceuticals  
INVENTOR(S): Desai, Neil P.; Tao, Chunlin; Yang, Andrew; Louie, Leslie; Yao, Zhiwen; Soon-Shiong, Patrick; Magdassi, Shlomo  
PATENT ASSIGNEE(S): American Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 112 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 19

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071079	A2	20001130	WO 2000-US13954	20000519 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6749868	B1	20040615	US 1999-316642	19990521
CA 2371912	A1	20001130	CA 2000-2371912	20000519 <--
AU 200050359	A	20001212	AU 2000-50359	20000519 <--
AU 784416	B2	20060330		
EP 1178786	A1	20020213	EP 2000-932669	20000519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 2006202836	A1	20060727	AU 2006-202836	20060630
PRIORITY APPLN. INFO.:				
		US 1999-316642	A2	19990521
		US 1993-23698	A2	19930222
		US 1995-412726	A2	19950329
		US 1996-720756	A3	19961001
		US 1998-198082	B2	19981123
		AU 2000-50359	A	20000519
		WO 2000-US13954	W	20000519

AB Compns. and methods useful for the in vivo delivery of water-insol. drugs (e.g., anticancer paclitaxel) in which the drug agent is delivered in the form of suspended particles coated with protein (which acts as a stabilizer) are described. In particular, protein and the drug in a biocompatible dispersing medium are subjected to high shear, in the absence of any conventional surfactants, and also in the absence of any polymeric core material for the particles. The procedure yields particles with a diameter of <1  $\mu$ . The use of specific composition and preparation conditions

(e.g., addition of a polar solvent to the organic phase), and careful election of the proper organic phase and phase fraction, enables the reproducible production of unusually small nanoparticles of less than 200 nm diameter, which can be sterile-filtered. The particulate system produced can be converted into a redispersible dry powder comprising nanoparticles of water-insol. drug coated with a protein, and free protein to which mols. of the drug are bound. This results in a unique delivery system, in which part of the drug is readily bioavailable (in the form of mols. bound to the protein), and part of the drug is present within particles without any polymeric matrix. Thus, 20 mg paclitaxel is dissolved in 1.0 mL methylene chloride and the solution mixed with 4.0 mL human serum albumin solution. The mixture was homogenized in order to form a crude emulsion and then sonicated. The dispersion was further lyophilized for 48 h without adding any cryoprotectant. The particle size after reconstitution was the same as before lyophilization.

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:441453 CAPLUS

DOCUMENT NUMBER: 129:180032

TITLE: Arterial uptake of biodegradable nanoparticles

AUTHOR(S) : for intravascular local drug delivery: Results with an acute dog model  
Song, Cunxian; Labhasetwar, Vinod; Cui, Xumin;  
Underwood, Thomas; Levy, Robert J.

CORPORATE SOURCE: Department of Pediatrics and Communicable Diseases,  
The University of Michigan Medical School, Ann Arbor,  
MI, USA

SOURCE: Journal of Controlled Release (1998), 54(2),  
201-211.  
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Biodegradable nanoparticles (NP) with a spherical diameter ranging from 70 to 160 nm were investigated for potential usefulness for the local intraluminal therapy of restenosis, the disease process responsible for arterial reobstruction following angioplasty. NPs containing a water-insol. anti-proliferative agent U-86983 (U-86, Pharmacia and Upjohn, Kalamazoo, MI) were formulated from oil-water emulsions using biodegradable polymers such as poly(lactic acid-glycolic acid) (PLGA), and specific additives after particle formation, to enhance arterial retention using either heparin, didodecylmethylammonium bromide (DMAB), or fibrinogen, or combinations. Femoral and carotid arteries of male mongrel dogs were isolated *in situ*, and were then subjected to a balloon angioplasty. A NP suspension of a predetd. concentration was then infused into the artery for various durations. This was followed by a 30 min restoration of blood flow through the vessel. The arterial segments were excised and analyzed for drug levels. From the drug loading of the NP and the drug levels in the artery, the quantity of nanoparticles retained was calculated and expressed as µg per 10 mg dry arteries. In general, repeated short infusions of nanoparticle suspension (15 s+4) were two-fold more effective in terms of higher arterial U-86 levels than a single prolonged infusion (60 s). A single 15 s infusion was not significantly different than a 60 s infusion on NP arterial uptake. NPs modified with either DMAB or fibrinogen had about 2.5-fold higher uptake levels compared to non-modified NPs ( $39.2 \pm 2.5$  and  $49.1 \pm 2.4$  vs.  $21.5 \pm 0.6$ , µg/10 mg mean+s.e., resp.). A comparably enhanced NP uptake was noted with a combined heparin/DMAB modification. Increasing the concentration of NP in infusate from 5 to 30 mg ml-1 significantly increased arterial NP uptake level (from  $22.5 \pm 3.5$  to  $83.7 \pm 1.4$  µg/10 mg). Thus, the results support the view that modified nanoparticles along with optimized infusion conditions could enhance arterial wall drug concns. of agents to treat restenosis.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 1998:407312 CAPLUS  
DOCUMENT NUMBER: 129:140595  
TITLE: Preparation and study of the characteristics of dithranol:polyvinylpyrrolidone coevaporates  
AUTHOR(S) : Delneuville, I.; Dechesne, J. P.; Delattre, L.  
CORPORATE SOURCE: Institute of Pharmacy, Laboratory of Pharmaceutical Technology, University of Liege, Liege, B-4000, Belg.  
SOURCE: International Journal of Pharmaceutics (1998), 168(1), 109-118  
CODEN: IJPHDE; ISSN: 0378-5173  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Dithranol:polyvinylpyrrolidone (Di:PVP) 1:2, 1:4, 1:9, 1:14, 1:25 and 1:40 coevaporates were prepared to increase the aqueous dispersibility of this hydrophobic and water insol. drug, used for the topical treatment of psoriasis. The coevaporates contained small crystals

of Di as well as nanoparticles of Di, embedded in the PVP matrix. This submicron fraction increased with increasing PVP, up to a Di:PVP ratio of 1:25. The coevaporates exhibited a hydrophilic character, allowing easy dispersion in water. This dispersion contained very small particles of submicron size (average diameter 0.1 μm) and an insol. part consisting of small Di crystals. When the insol. fraction was eliminated by filtration, an aqueous stable colloidal dispersion of Di was obtained. This extreme particle size reduction, combined with an enhanced hydrophilic character should provide Di with interesting characteristics for topical treatment of psoriasis.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 1997:501239 CAPLUS  
 DOCUMENT NUMBER: 127:113374  
 TITLE: Stabilized nanoparticles capable of being filtered under sterile conditions  
 INVENTOR(S): Verrecchia, Thierry  
 PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.; Verrecchia, Thierry  
 SOURCE: PCT Int. Appl., 20 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9722337	A1	19970626	WO 1996-FR2015	19961218 <--
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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EP 869776	A1	19981014	EP 1996-942419	19961218 <--
EP 869776	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000501989	T	20000222	JP 1997-522546	19961218 <--
AT 265848	T	20040515	AT 1996-942419	19961218
PT 869776	T	20040930	PT 1996-942419	19961218
ES 2219704	T3	20041201	ES 1996-942419	19961218
US 6139870	A	20001031	US 1998-94909	19980612 <--
PRIORITY APPLN. INFO.:			FR 1995-15033	A 19951219
			WO 1996-FR2015	W 19961218

AB Stabilized nanoparticles can be filtered under sterile conditions and including at least 1 hydrophobic, water-insol. and non-water-dispersible polymer or copolymer (and optionally an active principle) emulsified in a solution of phospholipids and an oleic acid salt. Thus, 750 mg of a diblock copolymer from poly(lactic acid) (mol. weight 30 kD) and PEG (mol. weight 2 kD) was dissolved in 20 mL EtOAc (solution A). Lecithin (175 mg) and 90 mg Na oleate were dispersed in 50 mL glucose soln (solution B). The solution A was emulsified in the solution B and homogenized for 10 min at 10°. The EtOAc was removed under reduced pressure to give a 45-mL suspension. The suspension was filtered and shown to be sterilized. The diameter of the particles was 63 nm.